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Attorney Docket No.: 24852-501 CIP3

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT(S): Bacopoulos et al.      CONFIRMATION NUMBER: 6445  
SERIAL NUMBER: 10/650,025      EXAMINER: PHYLLIS G. SPIVACK  
FILING DATE: August 26, 2003      ART UNIT: 1614  
FOR: **METHODS OF TREATING MESOTHELIOMA WITH  
SUBEROYLANILIDE HYDROXAMIC ACID**

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**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, Applicants hereby make of record the documents listed on the enclosed Modified Form 1449/PTO in the above-identified patent application. In accordance with MPEP §609(III)(A)(2), copies of the cited U.S. patents and publications are not required.

This Information Disclosure Statement is being filed concurrently with a Request for Continued Examination (RCE) and a Petition to Withdraw from Issue After Payment of Issue Fee Under 37 C.R.R. § 1.313(c)(2). Accordingly, no fee is considered due.

It is respectfully requested that the Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims, and signs the enclosed form PTO-1449 to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application.

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information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

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Respectfully submitted,

Dated: April 14, 2006



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Modified Form 1449/PTO  <b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)	<b>Application Number</b>	10/550,025
	<b>Filing Date</b>	August 26, 2003
	<b>First Named Inventor</b>	Bacopoulos, et al.
	<b>Group Art Unit / Conf. No.</b>	1614 / 6445
	<b>Examiner Name</b>	Phyllis G. Spivack
	<b>Attorney Docket Number</b>	24852-501 CIP3

U.S. PATENT DOCUMENTS							
Exam Initials	Cite No.	U.S. Patent Document No.	Issue Date	Name of Patentee(s) or Applicant(s)	Class	Sub Class	Filing Date if Appropriate
	A25	4,690,918	09/01/87	Beppu, et al.			
	A26	5,654,333	08/05/97	The United States of America as represented by the Department of Health and Human Services			
	A27	6,239,176	05/29/01	Beacon Laboratories, Inc. et al.			
	A28	6,262,116	07/17/01	Sloan-Kettering Institute for Cancer Research			
	A29	6,451,334	09/17/02	Perrine			
	A30	6,495,719	12/17/02	CircaGen Pharmaceutical			
	A31	2003/0114525	06/19/03	Kammer, et al.			
	A32	2004/0132643	07/08/04	Fojo, et al.			
	A33	2004/0167184	08/26/04	Wiech, et al.			

FOREIGN PATENT DOCUMENTS						
Exam Initials	Cite No.	Foreign Patent Document Office Number	Name of Patentee(s) or Applicant(s)	Date of Publication	English Yes	English No
	B14	WO 98/39965	Beacon Laboratories, LLC	09/17/98	X	
	B15	WO 02/15921	The Government of the United States of America	02/28/02	X	
	B16	WO 02/055017	Wake Forest University	07/18/02	X	

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS							
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.					
	C86	"Aton Pharma, Inc. Announces Initiation of Two Phase II Trials to Evaluate Efficacy of HDAC Inhibitor SAHA", October 30, 2002.					
	C87	"Aton Pharma, Inc. Announces Phase I Clinical Trial of SAHA in Advanced Leukemias", July 1, 2003.					
	C88	"Aton Pharma, Inc. Appoints Judy H. Chiao, M.D., as Vice President, Oncology Clinical Research and Development", September 20, 2002.					
	C89	"Aton Pharma, Inc. Presents Phase I Trial Data of Anti-Cancer Agent SAHA in Patients with hematological Malignancy at ASCO", June 2, 2003.					
	C90	"Aton Pharma, Inc. Presents Phase I Trial Data on Anti-Cancer Agent SAHA at EORTC/NCI/AACR Symposium", November 21, 2002.					
	C91	"Aton Pharma, Inc. Received Orphan Drug Designation for SAHA in Multiple Myeloma and Initiates Phase I Trial", October 13, 2003.					
	C92	"Aton Pharma, Inc. Reports on Phase I Trial of SAHA", August 14, 2002.					
	C93	Adhikari, D et al., Proceedings of the American Association for Cancer Research Annual Meeting, (1998), Vol. 39, p 312, "Radiosensitization of Lymphoma Cell Lines by Sodium Butyrate".					

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C94	Alexandrov, I et al., FEBS Letters, (1998), Vol. 434, pp 209-214, "Sodium Butyrate Suppresses Apoptosis In Human Burkitt Lymphomas and Murine Plasmacytomas Bearing c-myc Translocations".
	C95	Almenara, J et al., Leukemia (2002), Vol. 16, pp 1331-1343, "Synergistic Induction of Mitochondrial Damage and Apoptosis in Human Leukemia Cells by Flavopiridol and the Histone Deacetylase Inhibitor Suberoylanilide Hydroxamic Acid (SAHA)".
	C96	Amin HM et al., British Journal of Haematology (2001), Vol. 115, pp 287-297, "Histone Deacetylase Inhibitors Induce Caspase-Dependent Apoptosis and Downregulation of Daxx in Acute Promyelocytic Leukaemia with t(15;17)".
	C97	Aron, JL et al., Blood (2003), Vol. 102, No. 2, pp 652-658, "Depsipeptide (FR901228) Induces Histone Acetylation and Inhibition of Histone Deacetylase in Chronic Lymphocytic Leukemia Cells Concurrent With Activation of Caspase 8-mediated Apoptosis and Down-Regulation of c-FLIP Protein".
	C98	Benoit, NE et al., Immunopharmacology, (1996), Vol. 35, pp 129-139, "Increased inhibition of Proliferation of Human B Cell Lymphomas Following Litigation of CD40, and Either CD19, CD20, CD95 or Surface Immunoglobulin".
	C99	Bode, J et al., Journal of Interferon Research, (1982), Vol. 2, No. 2, pp 159-166, "Links Between Effects of Butyrate on Histone Hyperacetylation and Regulation of Interferon Synthesis in Namalva and FS-4 Cell Lines".
	C100	Buckley, AR et al., Cell Growth & Differentiation (1996), Vol. 7, pp 1713-1721, "Alterations in pim-1 and c-myc Expression Associated with Sodium Butyrate-Induced Growth Factor Dependency in Autonomously Growing Rat Nb2 Lymphoma Cells".
	C101	Buckley, AR et al., Proceedings of the American Association for Cancer Research Annual Meeting, (1997), Vol. 38, p 193, "Reversal of Apoptosis Resistance by Butyrate in rat Nb2 Lymphoma Cells".
	C102	Byrd, JC et al., Blood (1999), Vol. 94, No. 4, pp 1401-1408, "Depsipeptide (FR901228): A Novel Therapeutic Agent with Selective, In Vitro Activity Against Human B-Cell Chronic Lymphocytic Leukemia Cells".
	C103	Carducci, MA et al., Clinical Cancer Research (2001), Vol. 7, No. 10, pp 3047-3055, "A Phase I Clinical and Pharmacological Evaluation of Sodium Phenylbutyrate on an 120-h Infusion Schedule".
	C104	Dear, AE et al., Biochimica et Biophysica Acta, (2000), Vol. 1492, pp 15-22, "The Novel Anti-Tumour Agent Oxamflatin Differentially Regulates Urokinase and Plasminogen Activator Inhibitor Type 2 Expression and Inhibits Urokinase-Mediated Proteolytic Activity".
	C105	Desai, D et al., Anticancer Research (2003), Vol. 23, pp 499-504, "Chemopreventive Efficacy of Suberoylanilide Hydroxamic Acid (SAHA) Against 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-induced Lung Tumorigenesis in Female A/J Mice".
	C106	Dhordain, P et al., Nucleic Acids Research, (1998), Vol. 26, No. 20, pp 4645-4651, "The LAZ3(BCL-6) Oncoprotein Recruits a SMRT/mSIN3A/Histone Deacetylase Containing Complex to Mediate Transcriptional Repression".
	C107	Edelman, MJ et al., Cancer Chemotherapy and Pharmacology (2003), Vol. 51, pp 439-444, "Clinical and Pharmacologic Study of Tributyrin: An Oral Butyrate Prodrug".
	C108	Feinman, R et al., Blood (2002), Vol. 100, No. 11, pp Abstract 3195, "The Histone Deacetylase Inhibitor, Suberoylanilide Hydroxamic Acid, Induces Apoptosis of Multiple Myeloma Cells".
	C109	Filipovich, I et al., Biochemical and Biophysical Research Communications, (1994), Vol. 198, pp 257-265, "Butyrate Induced Apoptosis in Lymphoid Cells Preceded by Transient Over-Expression of HSP70 mRNA".
	C110	Foss, FM et al., Blood, (1993), Vol. 82, No. 10, Suppl. 1, p 564A, "Biomodulatory Effects of Butyric Acid Derivatives on Leukemia and Lymphoma Cells".
	C111	Gelmetti, V et al., Molecular and Cellular Biology (1998), Vol. 18, No. 12, pp 7185-7191, "Aberrant Recruitment of the Nuclear Receptor Corepressor-Histone Deacetylase Complex by the Acute Myeloid Leukemia Fusion Partner ETO".
	C112	Gerbitz, A, Oncogene, (1999), Vol. 18, pp 1745-1753, "Deregulation of the Proto-Oncogene c-myc Through t(8;22) Translocation in Burkitt's Lymphoma".
	C113	Gilbert, J et al., Clinical Cancer Research (2001), Vol. 7, No. 8, pp 2292-2300, "A Phase I Dose Escalation and Bioavailability Study of Oral Sodium Phenylbutyrate in Patients with Refractory Solid Tumor Malignancies".
	C114	Grisolano, JL et al., Proceedings of the National Academy of Sciences (2003), Vol. 100, No. 16, pp 9506-9511, "An Activated Receptor Tyrosine Kinase, TEL/PDGFBetaR, Cooperates with AML1/ETO to Induce Acute Myeloid Leukemia in Mice".

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C115	Harris, NL et al., Blood (1994), Vol. 84, No. 5, pp 1361-1392, "A Revised European-American Classification of Lymphoid Neoplasms: A Proposal From the International Lymphoma Study Group".
	C116	Jaboin, J et al., Cancer Research (2002), Vol. 62, No. 21, pp 6108-6115, "MS-27-275, an Inhibitor of Histone Deacetylase, Has Marked in Vitro and in Vivo Antitumor Activity against Pediatric Solid Tumors".
	C117	Kurita-Ochial, T et al., Infection and Immunity, (1998), Vol. 66, No. 6, pp 2587-2594, "Volatile Fatty Acid, Metabolic By-Product of Periodontopathic Bacteria, Induces Apoptosis in WEHI 231 and RAJI B Lymphoma Cells and Splenic B Cells".
	C118	Liu, Z et al., Journal of Cancer Research and Clinical Oncology, (1998), Vol. 124, pp 541-548, "Synergistic Effect of Epstein-Barr Virus and Tumor Promoters on Induction of Lymphoma and Carcinoma in Nude Mice".
	C119	Madisen, L et al., Molecular and Cellular Biology, (1998), Vol. 18, No. 11, pp 6281-6292, "The Immunoglobulin Heavy Chain Locus Control Region Increases Histone Acetylation along Linked c-myc Genes".
	C120	Niitsu, N et al., Molecular Pharmacology, (2000), Vol. 58, pp 27-36, "Anticancer Derivative of Butyric Acid (Pivaloyloxymethyl Butyrate) Specifically Potentiates the Cytotoxicity of Doxorubicin and Daunorubicin Through the Suppression of Microsomal Glycosidic Activity".
	C121	Orr, D et al., 2000 ASCO Annual Meeting, Abstract No. 763, "Phase I Pharmacokinetic (PK) Study of CI-994 in Combination with Gemcitabine (GEM) in Patients with Advanced Solid Tumors".
	C122	Polack, A et al., The EMBO Journal, (1993), Vol. 12, No. 10, pp 3913-3920, "Regulatory Elements in the Immunoglobulin Kappa Locus Induce c-myc Activation and the Promoter Shift in Burkitt's Lymphoma Cells".
	C123	Rezuze, WN et al., Clinical Chemistry (1997), Vol. 43, No. 10, pp 1814-1823, "Molecular Diagnosis of B- and T-cell Lymphomas: Fundamental Principles and Clinical Applications".
	C124	Rottlieb, C et al., International Journal of Cancer, (1995), Vol. 62, pp 697-702, "Among 17 Inducers of Differentiation Only Sodium Butyrate Causes a Permanent Down-Regulation of c-myc in Burkitt's Lymphoma".
	C125	Rottlieb, C et al., International Journal of Cancer, (1996), Vol. 67, pp 724-729, "Structure-Activity Relationship of 17 Structural Analogues of N-Butyric Acid Upon c-myc Expression".
	C126	Rubio, MA et al., Blood, (1995), Vol. 86, No. 10, pp 3715-3724, "Granulocyte-Macrophage Colony-Stimulating Factor, Phorbol Ester, and Sodium Butyrate Induce the CD11c Integrin Gene Promoter Activity During Myeloid Cell Differentiation".
	C127	Schrump, DS et al., Clinical Lung Cancer (2002), Vol. 4, No. 3, pp 186-192, "Phase I Study of Sequential Deoxyazacytidine/depsipeptide infusion in Patients with Malignancies Involving Lungs or Pleura".
	C128	Vrana JA et al., Oncogene (1999), Vol. 18, pp 7016-7025, "Induction of Apoptosis in U937 Human Leukemia Cells by Suberoylanilide Hydroxamic Acid (SAHA) Proceeds Through Pathways That are Regulated by Bcl-2/Bcl-XL, c-Jun, and p21 <sup>CIP1</sup> , but independent of p53".
	C129	Watanabe, M et al., Cancer Research (1990), Vol. 50, pp 3245-3248, "Effect of liposomes containing sodium butyrate conjugated with anti-CD19 monoclonal antibody on in vitro and in vivo growth of malignant lymphoma".
	C130	Yu, C et al., Cancer Research (2001), Vol. 63, pp 2118-2126, "Histone Deacetylase Inhibitors Promote ST1571-Mediated Apoptosis in ST1571-Sensitive and -Resistant Bcr/Abl Human Myeloid Leukemia Cells".
	C131	Zhang, M et al., Cell Stress & Chaperones, (1998), Vol. 3, No. 1, pp 57-66, "Heat-Induced Proteolysis of HSF Causes Premature Deactivation of the Heat Shock Response in Nb2 Lymphoma Cells".

\* a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. \_\_\_\_\_, filed \_\_\_\_\_, and relied upon for an earlier filing date under 35 U.S.C. §120 (continuation, continuation-in-part, and divisional applications).

Examiner Signature	Date Considered
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